JACC Vol. 8, No. 1
July 1986:11–7



CLINICAL STUDIES

# Plasma Norepinephrine in Exercise-Induced Ventricular Tachycardia

NEIL M. SOKOLOFF, MD, SCOTT R. SPIELMAN, MD, FACC,
ALLAN M. GREENSPAN, MD, FACC, ALAN P. RAE, MD, R. STEPHEN PORTER, PHARM D,
DAVID T. LOWENTHAL, MD, A.-HAMID HAKKI, MD, FACC,
ABDULMASSIH S. ISKANDRIAN, MD, FACC, HAROLD R. KAY, MD,
LEONARD N. HOROWITZ, MD, FACC

*Philadelphia, Pennsylvania*

**The relation between plasma norepinephrine levels and the occurrence of ventricular tachycardia during exercise testing was prospectively evaluated in 17 patients. Ten patients had reproducible ventricular tachycardia exclusively during exercise or recovery, or both; 7 patients had ventricular tachycardia only during ambulatory electrocardiographic monitoring. The two groups did not differ in age, exercise duration, left ventricular ejection fraction at rest, heart rate throughout the exercise protocol, rest QTc interval, change in QTc interval during exercise, the presence of coronary artery disease or exercise-related myocardial ischemia. Furthermore, there was no difference between groups in plasma norepinephrine levels at rest, peak exercise or in the recovery period. Myocardial ischemia was detectable by thallium perfusion scan in only 2 of the 10 patients with exercise-induced ventricular tachycardia.**

**The 10 patients with exercise-induced ventricular tachycardia underwent repeat exercise testing immediately after maximal intravenous beta-adrenergic blockade with propranolol. Although they had no change in exercise duration, ventricular tachycardia did not occur in 9 of these 10 patients. Plasma norepinephrine levels were significantly decreased compared with levels before beta-adrenergic blockade ($p < 0.0002$).**

**Thus, plasma norepinephrine levels do not distinguish patients with reproducible exercise-induced ventricular tachycardia from otherwise comparable patients. Propranolol is highly effective in abolishing this arrhythmia and this effect is associated with decreased norepinephrine levels.**

***(J Am Coll Cardiol 1986;8:11–7)***

The occurrence of ventricular ectopic activity and ventricular tachycardia during exercise testing has been the subject of considerable investigation over the last decade. Terms such as exercise-induced ventricular ectopic activity/ventricular tachycardia or catecholamine-induced ventricular ectopic activity/ventricular tachycardia have been used to describe this phenomenon; however, these are often variably interpreted.

In one sense the term exercise-induced ventricular tachycardia has been used to describe an uncommon, variably reproducible disorder occurring primarily in young to middle-aged men without significant coronary artery disease, who have minimal or no ventricular dysfunction and generally have a good prognosis. It has been assumed that in this group elevated plasma catecholamine levels play a major role in the pathogenesis of this disorder and that beta-adrenergic blockade provides effective symptomatic relief. Therefore, the aim of this study was to prospectively evaluate the relation of plasma catecholamines to the exercise-related induction of ventricular tachycardia.

## Methods

**Study patients.** Seventeen patients met the entrance criteria (see later) and constituted the study group. All patients signed informed written consent (protocol approved by the Hahnemann Institutional Review Board on June 8, 1982). The group consisted of normotensive subjects in whom all antiarrhythmic, beta-adrenergic blocking and calcium chan-

From the Likoff Cardiovascular Institute, Hahnemann University Hospital, Philadelphia, Pennsylvania. This study was supported in part by a grant from the American Heart Association, Southeastern Pennsylvania Chapter, Philadelphia, Pennsylvania.

Manuscript received August 30, 1985; revised manuscript received January 21, 1986, accepted February 7, 1986.

Address for reprints: Neil M. Sokoloff, MD, Cardiac Electrophysiology Laboratory, Department of Medicine, Allegheny General Hospital, 320 East North Avenue, Pittsburgh, Pennsylvania 15212.



0735-1097/86/$3.50

nel blocking medication was discontinued at least 5 half-lives before evaluation. Initially, all patients underwent a minimum of 48 hours of ambulatory electrocardiographic monitoring.

**Exercise testing.** The patients then underwent a post-absorptive state (8 hour) maximal symptom-limited treadmill test in accordance with the Bruce protocol (1). They were specifically instructed to avoid caffeine during the 8 hour period before testing. The exercise test was divided into three phases: a 5 minute observation period, an exercise period and a 10 minute recovery period. Patients were selected for a control group matched for age and left ventricular ejection fraction at rest (Group 1) if they manifested ventricular tachycardia (at least three consecutive ventricular complexes, greater than 100/min) during ambulatory monitoring and no ventricular tachycardia during the exercise or recovery periods. Patients were initially selected for the exercise-induced ventricular tachycardia group (Group 2) if they had ventricular tachycardia during graded exercise or recovery, or both. These patients were exercised again at least 24 hours later and remained in Group 2 only if ventricular tachycardia could be reproduced during the second test. Patients who had ventricular tachycardia during both ambulatory monitoring and exercise testing were excluded from the study. Forms of ventricular ectopic activity other than ventricular tachycardia were not considered. Ten patients were included in Group 2, and 7 patients were included in Group 1 (the control group). One potential Group 2 patient with exercise-induced ventricular tachycardia was excluded because of nonreproducibility.

**Clinical evaluation.** All patients had first pass radionuclide angiography at rest and two-dimensional echocardiography (to exclude mitral valve prolapse) as part of their evaluation. Coronary artery disease was considered present if there was an electrocardiographically documented myocardial infarction (two Group 2 patients, two Group 1 patients) or if coronary angiography demonstrated at least 50% luminal narrowing of the left main coronary artery or a minimum of 70% narrowing of at least one major coronary artery (two Group 2 patients, one Group 1 patient).

*Thallium-201 imaging* was performed in conjunction with the exercise test for all Group 1 patients and was performed with the second exercise test for all Group 2 patients. Electrocardiographic leads $V_3$, $V_5$ and aVF were monitored continuously during exercise testing. A 6 second delay circuit allowed recall of electrocardiographic events before the occurrence of ventricular tachycardia. Exercise end points were severe chest pain, dyspnea, fatigue, lightheadedness or 2 mm or more of horizontal or downsloping ST segment depression relative to baseline. Ventricular ectopic activity of any form, including ventricular tachycardia, was not cause for exercise termination unless it was associated with significant symptoms.

*In addition, a two channel Holter ambulatory electrocardiographic recording (modified leads $V_1$ and $V_5$)* was obtained for at least 15 minutes before exercise, during exercise and for at least 1 hour after exercise. Blood pressure was determined by arm cuff sphygmomanometry.

*Exercise duration* was measured and graded in minutes according to the standard Bruce protocol, and other related variables were measured in all patients at rest, peak exercise and 1, 2, 5 and 10 minutes into recovery. These measurements were made with the patient standing, at rest, peak exercise and 1 minute into recovery. The 2 and 5 minute recovery measurements were made in the sitting position and the 10 minute measurement was made in the supine position. The variables evaluated included sinus rate, the QTc interval measured from the surface electrocardiogram and calculated using Bazett's formula (2) (measured QT interval in seconds divided by the square root of the RR interval in seconds) and the presence of a ventricular tachycardia event. A ventricular tachycardia event was recorded as having occurred at the closest measurement interval (peak exercise, 1, 2, 5 or 10 minutes into recovery). Tachycardia during exercise or within 30 seconds of cessation of exercise was recorded as having occurred at peak exercise. Tachycardia occurring 30 to 90 seconds after cessation of exercise was recorded as having occurred at 1 minute into recovery. Samples for plasma catecholamine levels were obtained from an indwelling 18 gauge antecubital vein catheter at each of the measurement intervals.

*At peak exercise, 2 mCi of thallium-201 was injected through the intravenous catheter.* The patient continued to exercise for 30 to 60 seconds (during which time the sample for peak exercise plasma catecholamine level was obtained). Ten minutes after peak exercise, thallium images were obtained in three projections. In all patients delayed imaging was performed at 4 hours after exercise. The technique of thallium imaging and the interpretation of results have been described previously (3).

**Repeat exercise after propranolol.** All Group 2 patients agreed to have exercise testing repeated after maximal intravenous beta-adrenergic blockade. Immediately before exercise, propranolol (0.2 mg/kg body weight) in solution with 50 cc of 5% dextrose in water was administered at a rate of 1 to 2 mg/min with continuous electrocardiographic monitoring. The standardized isoproterenol sensitivity test described by Cleaveland et al. (4) was employed to assess the degree of beta-adrenergic blockade, and in each patient this was found to be maximal. The patient was then reexercised using an identical protocol. If the patient's initial exercise thallium study had revealed a defect interpreted as ischemia, thallium imaging in conjunction with exercise was repeated.

**Catecholamine assay.** Blood (10 ml) obtained at each of the prescribed measurement intervals was analyzed for catecholamine concentration using a high performance liq-

uid chromatographic/electrochemical detection method adapted from Mayer and Shoup (5). This method has been demonstrated to be faster than and as accurate as the more traditional radioenzymatic method (6–8). Catecholamines were extracted from 1 ml plasma aliquots with activated alumina and recovery efficiency was assessed with 3,4-dihydroxybenzylamine as the internal standard.

Quality control studies reveal an interday coefficient of variation of 3.2% and an intraday coefficient of 10.4% for norepinephrine and respective values of 6.2 and 10.7% for epinephrine. Limits of detection of norepinephrine and epinephrine are 60 and 30 pg/ml, respectively, with a signal to noise ratio equal to five.

*Because of the fragile nature of the samples a rigid protocol of collection, handling and storage was employed.* Visibly hemolyzed samples were discarded. Plasma samples were collected in B-D green top Vacutainer tubes containing sodium heparin, a chelator (ethylene glycol-bis[beta-aminoethyl ether]-N,N′-tetraacetic acid) and an antioxidant glutathione with pH adjusted to 7.0, all of which add to catecholamine stability during storage (−80°C).

**Statistical analysis.** Intergroup differences were compared using analysis of variance techniques. Intragroup variances were compared using a repetitive measures analysis of variance. In all analysis of norepinephrine levels a logarithmic transformation was done to normalize variance. In all cases a probability (p) value of 0.05 or less was considered significant. All results are expressed as the mean ± SEM or as the mean and the range.

**Table 1.** Study Patients

| Patient | Age (yr) & Sex | Cardiac Disease | Rest LVEF (%) |
|---|---|---|---|
| AMVT (Group 1) | | | |
| 1 | 38M | None | 60 |
| 2 | 53F | CAD | 44 |
| 3 | 55F | CAD | 45 |
| 4 | 44F | None | 58 |
| 5 | 37M | None | 60 |
| 6 | 53F | CAD | 44 |
| 7 | 68F | CM | 46 |
| Mean | 49.7 | | 51.0 |
| ± SEM | 4.1 | | 2.9 |
| EXVT (Group 2) | | | |
| 8 | 59F | CM | 48 |
| 9 | 69M | None | 68 |
| 10 | 40M | CAD | 56 |
| 11 | 58M | CAD | 61 |
| 12 | 36F | None | 62 |
| 13 | 67M | CAD | 33 |
| 14 | 62F | CM | 44 |
| 15 | 37M | None | 45 |
| 16 | 59F | CAD | 45 |
| 17 | 25M | CM | 37 |
| Mean | 51.2 | | 50.9 |
| ± SEM | 4.8 | | 3.6 |

AMVT = ventricular tachycardia on ambulatory electrocardiographic monitoring; CAD = coronary artery disease; CM = cardiomyopathy; EXVT = exercise-induced ventricular tachycardia; F = female; LVEF = left ventricular ejection fraction; M = male; None = no organic heart disease.

## Results

The demographic characteristics of the two groups were similar (Table 1). Three patients in each group had no evidence of organic heart disease. The remaining patients had either no or mild to moderate impairment of left ventricular function at rest.

**Exercise testing results (Table 2).** There was no difference between the two groups in exercise heart rate (Fig. 1) or exercise duration. All 17 patients exercised to fatigue; none had chest pain or other symptoms requiring termination of the test. Systolic blood pressure did not decrease in any patient, and no patient had a decrease in diastolic pressure of more than 10 mm Hg.

*Four Group 2 patients had ventricular tachycardia at peak exercise,* five had ventricular tachycardia during the recovery period and one had ventricular tachycardia during both exercise and recovery. There was no correlation between the occurrence of a ventricular tachycardia episode and any clinical or exercise characteristic. The ventricular tachycardia in each patient was of constant rate and uniform configuration; all had a left bundle branch configuration with a normal or right axis. The episodes appeared as bursts separated by at least one sinus complex and each began with a late coupled ventricular complex (greater than 50% of the preceding RR interval). The ventricular tachycardia rate ranged from 140 to 160 beats/min (mean 154) with less than 10% rate variation in an individual patient. The duration of ventricular tachycardia episodes ranged from three complexes to self-terminating long runs (more than 30 complexes) (Fig. 2). All ventricular tachycardia episodes were well tolerated by the patients, and at no time was medical intervention necessary.

*The QTc intervals at rest did not differ between the two groups.* The maximal QTc change was defined at peak exercise in Group 1 and just before the onset of ventricular tachycardia in Group 2. There was no correlation between change in QTc interval and occurrence of ventricular tachycardia.

*The results of thallium imaging are presented in Table 2.* Myocardial ischemia was detectable in 2 (20%) of 10 Group 2 patients and 1 (14%) of 7 Group 1 patients.

**Catecholamine results (Table 3).** Both norepinephrine and epinephrine levels were measured. Epinephrine levels are not reported because they were found to be at the lower limit of detection where the assay is relatively imprecise

**Table 2.** Exercise Test Results

| Patient | Exercise Duration (min) | QTc Rest/Change (s) | Thallium Result | First Occurrence of VT | Longest Episode of VT |
|---|---|---|---|---|---|
| AMVT (Group 1) | | | | | |
| 1 | 8.1 | 0.44/D | Normal | — | — |
| 2 | 9.0 | 0.39/D | Scar | — | — |
| 3 | 7.7 | 0.39/D | Ischemia | — | — |
| 4 | 17.0 | 0.30/D | Normal | — | — |
| 5 | 10.6 | 0.40/D | Normal | — | — |
| 6 | 6.6 | 0.48/D | Scar | — | — |
| 7 | 8.0 | 0.42/D | Normal | — | — |
| Mean | 9.6 | 0.41 | | | |
| ± SEM | 1.3 | 0.02 | | | |
| EXVT (Group 2): Baseline | | | | | |
| 8 | 7.7 | 0.42/N | Normal | + 1 min | 19S |
| 9 | 9.2 | 0.41/D | Normal | + 2 min | 5C |
| 10 | 9.0 | 0.41/D | Ischemia | Peak | 16C |
| 11 | 10.0 | 0.42/D | Scar | + 1 min | 7C |
| 12 | 14.3 | 0.44/D | Normal | + 5 min | 155S |
| 13 | 6.0 | 0.39/I | Scar | Peak | 8C |
| 14 | 5.0 | 0.45/D | Normal | Peak | 3C |
| 15 | 10.0 | 0.39/D | Normal | Peak | 19C |
| 16 | 4.4 | 0.32/I | Ischemia | + 1 min | 37C |
| 17 | 14.0 | 0.50/D | Scar | Peak | 5C |
| Mean | 9.0 | 0.41 | | | |
| ± SEM | 1.1 | 0.01 | | | |
| EXVT (Group 2): Beta-blockade | | | | | |
| 8 | 9.0 | 0.39/D | — | None | — |
| 9 | 9.9 | 0.40/D | — | Peak | 5C |
| 10 | 9.5 | 0.40/D | Normal | None | — |
| 11 | 12.2 | 0.36/I | — | None | — |
| 12 | 12.5 | 0.36/N | — | None | — |
| 13 | 6.0 | 0.37/I | — | None | — |
| 14 | 6.2 | 0.39/D | — | None | — |
| 15 | 10.1 | 0.40/I | — | None | — |
| 16 | 3.9 | 0.44/D | Normal | None | — |
| 17 | 14.0 | 0.41/D | — | None | — |
| Mean | 9.3 | 0.39 | | | |
| ± SEM | 1.0 | 0.01 | | | |

C = complexes; D = decrease; I = increase; N = no change; S = seconds; VT = ventricular tachycardia; other abbreviations as in Table 1.

(9). Norepinephrine levels (Fig. 3) were well above the limit of detection and closely paralleled the level of exercise. Peak norepinephrine levels occurred either at peak exercise (1 of 10 in Group 2, 1 of 7 in Group 1) or at 1 minute into recovery (9 of 10 in Group 2, 6 of 7 in Group 1).

*There was no difference in plasma norepinephrine levels between the groups.* In addition, there was no correlation between the onset of ventricular tachycardia and plasma norepinephrine levels.

**Effect of beta-blockade.** Repeat testing of Group 2 patients after maximal intravenous beta-adrenergic blockade with propranolol was performed 24 hours to 2 weeks subsequent to the previous test. Heart rate ($p < 0.0001$) (Fig. 1) and plasma norepinephrine levels ($p < 0.0002$) (Table 3, Fig. 3 and 4) were reduced after beta-blockade. There was no significant change in QTc interval at rest or in exercise duration, and ventricular tachycardia only occurred in 1 of 10 patients after beta blockade.

## Discussion

This study demonstrates that plasma norepinephrine levels do not differentiate patients with exercise-induced ventricular tachycardia from otherwise comparable patients in whom ventricular tachycardia occurs only during routine ambulatory monitoring. Nonetheless, propranolol does pre-

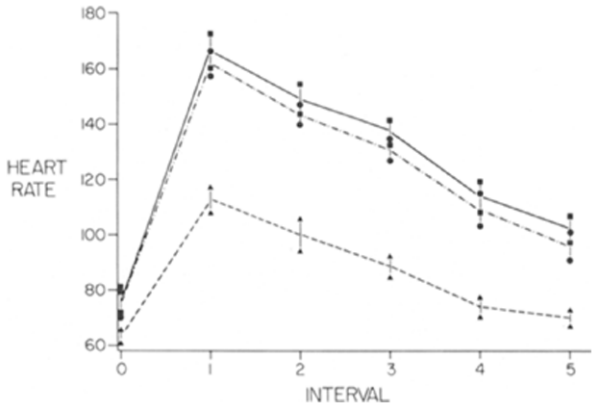


**Figure 1.** Heart rate during exercise testing. Mean sinus rate (**ordinate**) is plotted against time during the exercise protocol (**abscissa**). Intervals 0 through 5 correspond, respectively, to rest, peak exercise and 1, 2, 5 and 10 minutes' recovery. The **solid line** represents Group 1 (the control group), the **dash-dot line** represents Group 2 (the experimental group) during baseline testing and the **dashed line** represents Group 2 during testing after maximal beta-adrenergic blockade. SEM is indicated for each group at each interval. There is no difference in sinus rate between the two groups during the baseline exercise protocol. There is a significant decrease ($p < 0.0001$) in sinus rate in Group 2 after beta-blockade.

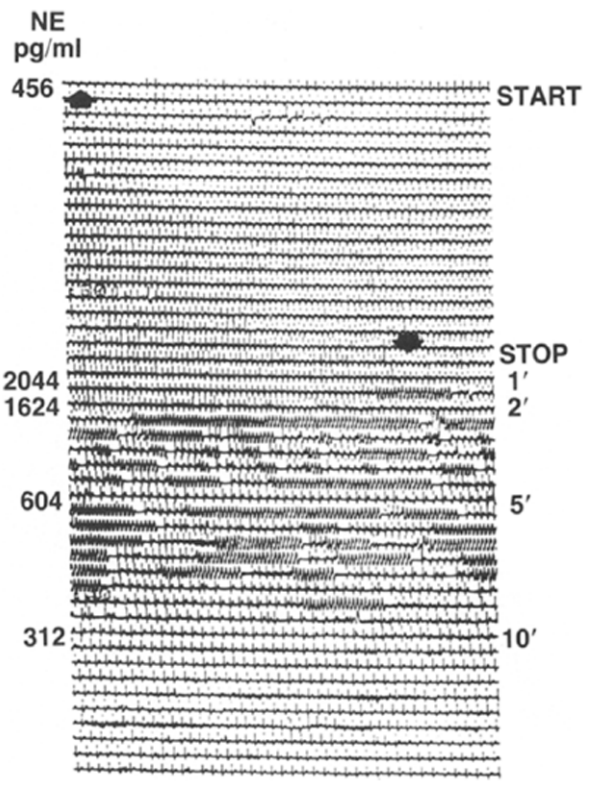


**Figure 2.** Exercise-induced ventricular tachycardia (Group 2). Continuous electrocardiographic recording (modified lead $V_1$) during baseline exercise testing. The **arrows** denote the start and peak of exercise. Plasma norepinephrine (NE) levels are shown on the **left** and correspond to discrete points in the exercise protocol shown on the **right**. A norepinephrine value is not available for peak exercise. Episodes of self-terminating ventricular tachycardia occur between 1 and 9 minutes of the recovery period.

vent exercise-induced ventricular tachycardia, although its mechanism of action is not clear.

**Possible mechanisms.** High concentrations of the catecholamine isoproterenol are known to induce or facilitate electrical induction of ventricular tachycardia in susceptible individuals in the electrophysiology laboratory (10–12). In the study by Sung et al. (10), in a heterogeneous population, a significant percent of what was termed exercise-induced ventricular tachycardia was reproducible in the electrophysiology laboratory only with infusion of catecholamine and not with programmed stimulation, suggesting a mechanistic link between exercise-induced ventricular tachycardia and catecholamines.

Although it was not the intent of this study to investigate the exact mechanisms producing exercise-induced ventricular tachycardia, we noted that most of our Group 2 patients manifested several characteristics of exercise-related ventricular tachycardia described by Wu et al. (13), such as a rapid succession of tachycardia episodes separated by at least one sinus complex, tachycardia rate in the range of 160/min, gradual resumption of sinus rhythm with a decrease in frequency and length of the episodes and prevention of the arrhythmia by beta-adrenergic blockade. Wu et al. postulated that "triggered activity" may be the underlying mechanism responsible for the arrhythmia. Cranefield (14) reported that norepinephrine increases the amplitude of afterdepolarizations or causes their appearance in vitro, a prerequisite for "triggered activity." In addition, Arnsdorf (15) found that beta-adrenergic blockade has a direct suppressive effect on such activity.

It has been suggested (16) that peripheral plasma norepinephrine levels continue to increase for several minutes after the cessation of exercise and that this might be the cause of life-threatening ventricular tachyarrhythmias. However, this discrepancy between peak exercise and peak

**Table 3.** Mean Plasma Norepinephrine Levels (pg/ml)

| | Rest | Peak Exercise | Recovery (min) +1 | +2 | +5 | +10 |
|---|---|---|---|---|---|---|
| AMVT (Group 1) | | | | | | |
| Mean | 298 | 2,054 | 1,885 | 1,368 | 839 | 744 |
| ± SEM | 30 | 302 | 243 | 130 | 70 | 117 |
| n | 7 | 7 | 7 | 7 | 7 | 7 |
| EXVT (Group 2): Baseline | | | | | | |
| Mean | 287 | 1,812 | 2,033 | 1,453 | 816 | 537 |
| ± SEM | 30 | 179 | 184 | 128 | 77 | 96 |
| n | 10 | 9 | 10 | 10 | 10 | 9 |
| EXVT (Group 2): Beta-Blockade | | | | | | |
| Mean | 235 | 1,370 | 1,227 | 1,014 | 743 | 527 |
| ± SEM | 35 | 151 | 157 | 113 | 113 | 79 |
| n | 10 | 9 | 9 | 10 | 10 | 10 |

n = number; other abbreviations as in Table 1.

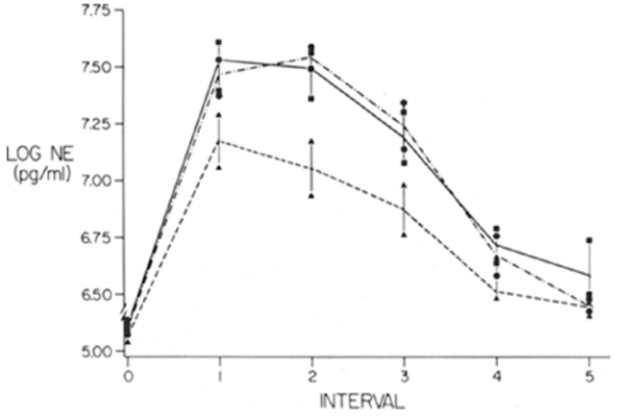


**Figure 3.** Mean plasma norepinephrine levels during exercise testing. Comparison of the logarithmic (LOG) transformation of mean plasma norepinephrine (NE) levels for Group 1 (the control group) (**solid line**), Group 2 (the experimental group) during baseline testing (**dash-dot line**) and Group 2 after maximal beta-blockade (**dashed line**). SEM is indicated for each group at each interval of the exercise protocol as in Figure 1. There is no difference in norepinephrine levels throughout the protocol between Group 1 and baseline Group 2; however, after maximal beta-adrenergic blockade, norepinephrine levels in Group 2 are significantly decreased ($p < 0.0002$).

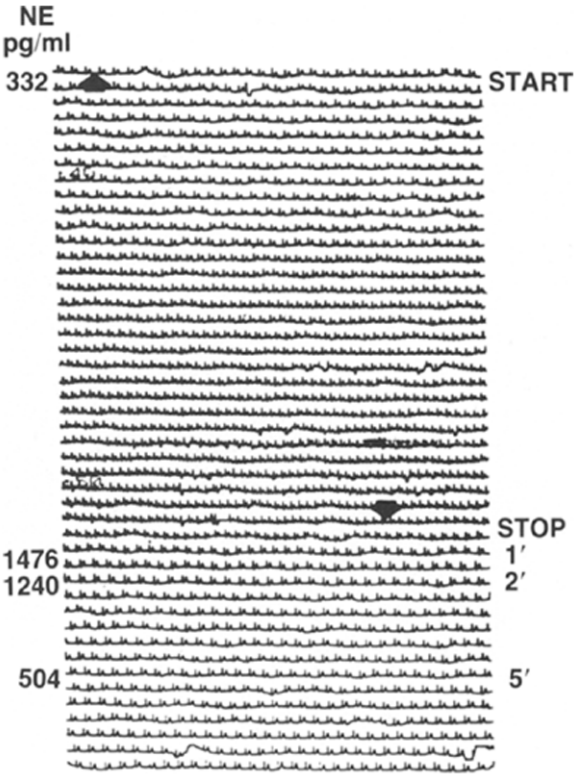


**Figure 4.** Exercise testing after beta-adrenergic blockade. Electrocardiographic records from the same patient as in Figure 2 after maximal beta-adrenergic blockade are shown with identical format. No episodes of ventricular tachycardia occur despite similar exercise duration.

norepinephrine levels is not surprising, because the majority of plasma norepinephrine is derived from nerve synapses, and there may be a lag time between what occurs at the synaptic level and what is detected peripherally. In our study, norepinephrine levels were maximal within 1 minute after peak exercise.

**Effect of beta-blockade.** The decrease in plasma norepinephrine levels after beta-adrenergic blockade with propranolol (Table 3, Fig. 3 and 4) has not been previously reported. We are not aware of a study employing similarly large doses of intravenous propranolol in patients. Sheehan et al. (17), utilizing oral doses that achieved plasma levels thought to be associated with effective beta-blockade in normal subjects during exercise, reported that propranolol blocks the action of norepinephrine at receptor sites but does not affect norepinephrine release. However, oral propranolol has significant first pass hepatic clearance (18) and large intravenous doses would be expected to result in substantially higher plasma levels. As it is unlikely that higher plasma propranolol levels would increase norepinephrine clearance, it appears that norepinephrine secretion is diminished. Because, in our study, exercise duration did not change after acute propranolol administration, this would not account for decreased norepinephrine secretion; and the postpropranolol abolition of previously reproducible ventricular tachycardia is further evidence that exercise-induced ventricular tachycardia is catecholamine mediated.

**Previous studies.** Woelfel et al. (19) also found that large doses of propranolol, administered orally (the degree of beta-blockade determined by peak sinus rate achieved during maximal exercise), were often required to prevent exercise induction of previously reproducible ventricular tachycardia; however, catecholamine levels were not reported. Our findings suggest that this effect of propranolol may be the result of decreased norepinephrine levels, receptor site blockade or a combination of the two.

Although our data are inferential they suggest that either plasma norepinephrine is not related to exercise-induced ventricular tachycardia or that these patients may be more sensitive to normal levels of norepinephrine released during maximal treadmill exercise testing. The latter concept is supported by the excellent response of the arrhythmia to beta-adrenergic blockade with propranolol, the lack of detectable plasma epinephrine in association with the arrhythmia and the frequent induction in susceptible individuals of ventricular tachycardia by catecholamine infusion.

Our experimental group (Group 2) is similar to patient groups evaluated by other researchers (13,19) in age, degree of left ventricular dysfunction (moderate to none), reproducibility of the arrhythmia (high), arrhythmia configuration and response to beta-adrenergic blockade (excellent). These patients may represent a distinct clinical group in which catecholamines are the predominant pathogenetic factor in

exercise-induced ventricular tachycardia, although such a clinical correlation has not been established.

In other studies (10,20,21) patients were generally older and had more severe cardiac disease, evaluation was not restricted to ventricular tachycardia (20) (as compared with more generalized ventricular ectopic activity) and the reproducibility of exercise induction of ventricular tachycardia was not carefully controlled (10,21). Arrhythmia pathogenesis in these patients is not clear and is likely to be multifactorial.

**Limitations.** It is not possible, on the basis of our data, to determine the exact mechanism by which propranolol abolishes exercise-induced ventricular tachycardia. We did not exercise the control group (Group 1) after maximal intravenous beta-adrenergic blockade and are therefore limited in evaluating norepinephrine levels after beta-blockade in the experimental group (Group 2). Also, to clarify propranolol's effect or effects it is necessary to separate its postsynaptic beta-adrenergic blocking action from the observed decrease in plasma norepinephrine levels. This might be accomplished by the administration of an agent such as reserpine which decreases plasma norepinephrine to patients with proven exercise-induced ventricular tachycardia.

**Conclusions.** We have demonstrated that patients with reproducible ventricular tachycardia that occurs exclusively during exercise testing have plasma norepinephrine levels similar to those of patients without this arrhythmia. Thus, patients with exercise-induced ventricular tachycardia may be more sensitive to plasma norepinephrine than are otherwise comparable patients. In 9 of 10 patients with exercise-induced ventricular tachycardia the arrhythmia was abolished by maximal beta-blockade. This blockade was associated with a decrease in plasma norepinephrine levels.

## References

1. Doan AE, Peterson DR, Blackmon JR, Bruce RA. Myocardial ischemia after maximal treadmill exercise in healthy men. A method for detecting potential coronary disease. Am Heart J 1965;69:11–20.
2. Bazett HC. An analysis of time-relations of electrocardiograms. Heart J 1920;7:353–70.
3. Iskandrian AS, Hakki AH. Thallium-201 myocardial scintigraphy. Am Heart J 1985;109:113–29.
4. Cleaveland CR, Rangno RE, Shand DG. A standardized isoproterenol sensitivity test. The effects of sinus arrhythmia, atropine and propranolol. Arch Intern Med 1972;130:47–52.
5. Mayer GS, Shoup RE. Simultaneous multiple electrode liquid chromatographic-electrochemical assay for catecholamines, indoleamines and metabolites in brain tissue. J Chromatogr 1983;255:533–44.
6. Causon RC, Carruthers ME, Rodnight R. Assay of plasma catecholamines by liquid chromatography with electrochemical detection. Anal Biochem 1981;116:223–6.
7. Krstulovic AM. Investigations of catecholamine metabolism using high-performance liquid chromatography. J Chromatogr 1982;229:1–34.
8. Hjemdahl P, Daleskog M, Kahan T. Determination of plasma catecholamines by high performance chromatography with electrochemical detection. Life Sci 1979;25:131–8.
9. Hjemdahl P. Inter-laboratory comparison of plasma catecholamine determinations using several different assays. Acta Physiol Scand 1984;527(suppl):43–54.
10. Sung RJ, Shen EN, Morady F, Scheinman MM, Hess D, Botvinick EH. Electrophysiologic mechanism of exercise-induced sustained ventricular tachycardia. Am J Cardiol 1983;51:525–30.
11. Reddy CP, Gettes LS. Use of isoproterenol as an aid to electric induction of chronic recurrent ventricular tachycardia. Am J Cardiol 1979;44:705–13.
12. Freedman RA, Swerdlow CD, Echt DS, Winkle RA, Soderholm-Difatte V, Mason JW. Facilitation of ventricular tachyarrhythmia by isoproterenol. Am J Cardiol 1984;54:765–70.
13. Wu D, Hwai-Cheng K, Hung JS. Exercise-triggered paroxysmal ventricular tachycardia. A repetitive rhythmic activity possibly related to afterdepolarization. Ann Intern Med 1981;95:410–4.
14. Cranefield PF. Action potentials, afterdepolarizations and arrhythmias. Circ Res 1977;41:415–23.
15. Arnsdorf MF. The effect of antiarrhythmic drugs on triggered sustained rhythmic activity in cardiac Purkinje fibers. J Pharmacol Exp Ther 1977;201;689–700.
16. Dimsdale JE, Hartley LH, Guiney T, Ruskin JN. Postexercise peril. Plasma catecholamines and exercise. JAMA 1984;251:630–2.
17. Sheehan MW, Brammell HL, Sable DL, Nies AS, Horowitz LD. Effect of beta adrenergic blockade on circulating catecholamines and dopamine-beta-hydroxylase activity during exercise in normal subjects. Am Heart J 1983;105;777–82.
18. Nies AS, Shand DG. Clinical pharmacology of propranolol. Circulation 1975;52:6–15.
19. Woelfel A, Forster JR, Simpson RJ, Gettes RS. Reproducibility and treatment of exercise-induced ventricular tachycardia. Am J Cardiol 1984;53:751–6.
20. Sami M, Kraemer H, DeBusk RF. Reproducibility of exercise-induced ventricular arrhythmia after myocardial infarction. Am J Cardiol 1979;43:724–30.
21. Motokoff DM, Quinones MA, Miller RR. Exercise-induced ventricular tachycardia. Clinical features, relation to chronic ventricular ectopy and prognosis. Chest 1980;77:10–6.